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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,266	09/25/2003	Byung Sook Moon	020048-004200US	8805

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EXAMINER	
PANDE, SUCHIRA	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,266	MOON ET AL.	
	Examiner	Art Unit	
	Suchira Pande	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 11, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *11,13-44,49 and 54-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12,45-48 and 50-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (Claims 1-12 & 45-53) and species election of polymerases along with the request for reconsideration of the restriction of Groups I, II and IV reciting beads, in the reply filed on May 11, 2006 is acknowledged. The traversal is on the ground(s) that mannitol is clearly a single inventive concept found in all the pending bead claims. This is not found persuasive because current application is filed under 35 U.S.C. 111 and has been restricted under 35 U.S.C. 121. The inventions are distinct under 37 C.F.R. 1.142 as pointed out in the office action mailed on April 18, 2006. Single inventive concept is applicable under 37 C.F.R. 1.475 to unity of invention before the International Searching Authority, the International Preliminary Examining Authority and during the national stage applications under 35 U.S.C. 371 and does not apply in the instant case. The requirement is still deemed proper and is therefore made FINAL.

Group I contained claims 1-12 & 45-53. Claims 11 and 49, are drawn to reverse transcriptase. In view of the species election of polymerases claims 11 and 49 are not being examined. Claims 1-10, 12, and 45-48, 50-53 are currently under examination in this application. Claims 7 and 48 are examined with respect to polymerase.

Specification

2. The use of the trademarks in pages 12, 16, 18 and 19 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 8 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The lyophilized bead of claims 1 and 45 are products and it is unclear how a methodology to perform a reaction "hot start methodology" provides further limitation to the product, as methodology is not a structural component of the product.

Claim Interpretation

4. Claims 8 and 50, as pointed out above are indefinite. The term "Hot Start Methodology" does not add any structural limitations to the claims. The two rejections for claims 8 and 50 are based on two different interpretations of the claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-8,10, 12, 45-48 and 50, 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et. al. 1999 US Pat. 5,861,251 and Treml et. al. 1998 US Pat. 5,763,157.

Claims 1 and 45 are being considered together because claim 45 is a product by process claim that shares the same structural components namely lyophilized bead suitable for use in amplification of a nucleic acid comprising a thermally stable enzyme and mannitol as recited in product of claim 1. The process steps (a-c in claim 45) are not being considered for search of prior art.

See MPEP 2113 [R1] PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

A) Regarding claims 1, 7, 8, 45, 48 and 50 Park et. al. teach:

a. A lyophilized reagent suitable for use in the amplification of a nucleic acid sequence, (see col. 1, lines 5-10, and col. 3, lines 1-10)

b. said lyophilized reagent comprising: a thermally stable enzyme (see col. 3, lines1-10). Park et. al. teach use of DNA Polymerase as the enzyme used for conducting amplification of nucleic acid using polymerase chain reaction where the enzyme is subjected to repeated cycling at high temperatures up to 94^0C. Hence the DNA polymerase used by them is thermally stable as it successfully performs DNA amplification as shown in examples 1-8 (see col. 3, lines 66-67; col. 4, 5 and 6 lines 1-67 of each).

c. And mannitol (see col. 3, line 27). Park et al. use mannitol as a stabilizer. Mannitol is part of their preferred stabilizers falling in the group

of polyols composed of glycerol, glucose, mannitol, galacitol, glucitol and sorbitol (see col. 3, lines 24-30).

Regarding claim 2, Park et. al. teaches amplification in a reaction mixture having a final volume of 50 μl (see col. 4, lines12-13 and lines 47-52).

Regarding claims 3 and 47, Park et. al. teaches dNTPs (see col.4, line 11) and mixture of ddNTPs and dNTPs (see col. 3, lines 1-10).

B) Regarding claims 1 and 45 Park et. al. do not teach:

d. A lyophilized bead wherein said lyophilized bead has a weight percentage of said mannitol of between about 53% and about 75% (w/w).

C) Regarding claims 1, 5-6, and 45 Treml et. al. teach:

e. A lyophilized bead referred to as biological reagent spheres by Treml et. al. suitable for use in the amplification of a nucleic acid sequence (see col. 3, lines 60-67; col. 4, lines 1-8 & col. 7, lines 23-35).

In case of Treml et. al. these beads are composed of a high molecular weight synthetic carbohydrate polymer and a second carbohydrate. Examples of second carbohydrate used by Treml et. al. includes polyols such as sorbitol. The lyophilized beads with weight percentage of second carbohydrate in the range of 5% to 15% expressed in (w/v) are taught by Treml et. al. (see col. 5, lines 49-52). Treml et. al. does not express the weight percentage of polyol in the beads in (w/w). Using the correspondence between % of mannitol in lyophilized beads described in Table 4 of the specification in w/v and w/w it is clear that 7% w/v of mannitol corresponds to 53.75 % w/w of mannitol in lyophilized

beads. Similarly 12.77 % w/v of mannitol would correspond to 75% w/w of mannitol in lyophilized beads. Both these numbers of w/v of mannitol namely 7-13 % are within the weight percentage range (5-15% w/v) for second carbohydrate polyol taught by Treml et. al.

Looking at the diameter of beads formed by using mannitol % expressed in w/v in Table 3 (see sizes of beads for 4.5 – 11% mannitol expressed in w/v in the specification) it is clear that these resulting beads are in the size range taught by Treml et. al. see the rejection for claims 4 and 46 below. This provides a further confirmation that the relationship derived between beads with % of mannitol expressed in w/v to w/w as described above is correct.

Hence lyophilized beads of claims 1, 5 and 6 having weight percentage of between about 53% and about 75% (w/w) as recited in claim 1; weight percentage of lyophilized bead between about 62% and about 75% (w/w) as recited in claim 5; and weight percentage of lyophilized bead between about 68% and about 75% (w/w) as recited in claim 6 are taught by Treml et. al.

Regarding claims 4 and 46, Treml et. al. teaches reagent spheres (lyophilized beads) with diameters of about 2 mm to about 6 mm. Preferably, the reagent sphere has a diameter of about 2.5 mm (see col. 3, lines 63-65). Thus lyophilized bead with an average cross-section of about 1 mm and about 4.5 mm are taught by Treml et. al.

Regarding claims 10 and 52, Treml et. al. teaches reagent spheres where the biological reagents are oligonucleotides, proteins, enzymes, DNA or nucleic acids (see co. 4, lines 7-8). All of these are employed as probes in the art for different purposes.

Regarding claims 12 and 53, Treml et. al. teaches reagent spheres where the biological reagent is selected from at least one of the group consisting of DNA/RNA modifying enzymes, restriction enzymes, nucleotides, oligonucleotides, proteins, enzymes, DNA or nucleic acids (see col. 4, lines 4-8). Different molecules may be used as internal control for different purposes. For example DNA could be used as internal control for amplification reactions, therefore Treml et. al. teaches a bead containing internal control.

As described above Park et. al specifically teach use of mannitol as a preferred polyol to be used for stabilizing lyophilized reagents to be used for nucleic acid amplification.

Hence it would have been obvious to one of ordinary skill in the art at the time of the present invention to use the lyophilized beads of Treml et. al. as the lyophilized reagent of Park et. al. for use in nucleic acid amplification. The motivation to use lyophilized beads as described by Treml et. al. as lyophilized reagent useful for amplification of nucleic acid taught by Park et. al. is provided by Treml et. al. who describe the limitations and drawbacks associated with the various methods such as dry-blending, spray drying, freeze drying, fluidized bed drying, and /or cryogenic freezing employed for producing dry biological reagents (see col. 1, lines 32-67; col. 2, lines 1-25; col. 3, lines 1-22). They further go on to

describe the advantages of their invention namely "providing a homogenous solution of biological reagent(s), glass forming filler material, and water-wherein the shape of droplets formed on an inert cryogenic surface can be controlled by changing the percent solids of emulsion ----------providing stable storage of a biological reagent that would otherwise be unstable when alone in an aqueous solution at room temperature and providing stable storage of a plurality of biological reagents that would otherwise react with each other when in an aqueous solution at room temperature" (see col.4, lines 51-67 and col. 5, lines 1-9).

8. Claims 8 and 50, are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et. al. and Treml et. al. as applied to claims 1 and 45 above, and further in view of Kellogg et. al. (1994) Biotechniques Vol. 16 (6) 1134-1137.

Regarding claim 8, Park et. al. and Treml et. al. does not teach a DNA polymerase that facilitates DNA amplification reactions using Hot Start Methodology.

Kellogg et. al. describe a Taq DNA Polymerase that when coupled to neutralizing TaqStartAntibody™, a monoclonal antibody (MAb) directed against Taq DNA polymerase facilitates "Hot start" PCR. (see page 1135, par. 3).

It would have been obvious to one of ordinary skill in the art to incorporate the Taq DNA Polymerase coupled to neutralizing TaqStartAntibody™, that facilitates "Hot start" PCR of Kellogg et. al. in the product of Park et. al. and Treml et. al. at the time of the claimed invention. The motivation to combine the

product of Kellogg et. al. in the product of Park et. al. and Treml et. al. is provided by Kellogg et. al. who state "To address the drawbacks inherent in the above methods, we have generated the TaqStartAntibody™, a monoclonal antibody (MAb) the deactivates Taq DNA polymerase at ambient temperature. Heating a reaction mixture to the denaturation temperature reverses the deactivation of the polymerase and permits the amplification to proceed in a specific and efficient manner. The results indicate that using the antibody greatly reduces non specific products and enhances yield of the specific product" (see page 1135, par. 3).

9. Claims 9 and 51, are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et. al. and Treml et. al. as applied to claims 1 and 45 above, and further in view of Shively et. al. March 2003 BioTechniques vol. 34: (3) pp. 498-504.

Regarding claims 9 and 51, Park et. al. teaches a reaction buffer (see col. 2, line 1) that must be part of the reaction mixture before amplification of nucleic acids can take place by PCR. But neither Park et. al. nor Treml et. al. teaches use of buffer HEPES in DNA amplification.

Shively et. al. teaches use of HEPES buffer in amplification reactions used to perform Real –Time PCR assay for quantitative mismatch detection. (see page 498 abstract). They describe an assay suitable for quantitative detection of single-base-pair differences that does not require fluorescently labeled gene specific probes. The method requires use of HEPES buffer at a pH of 6.95 together with Ampli-Taq® DNA polymerase results in a threshold difference

between the correct template and the mismatched template of as many as 20 cycles, depending on the mismatch. (see page 498, abstract).

It would have been obvious to one of ordinary skill in the art to incorporate the buffer of Shively et. al. in the product of Park et. al. and Treml et. al. The motivation to combine the buffer of Shively et. al. in the product of Park et. al. and Treml et. al. is provided by Shively et. al. who state " the technique we describe allows more accurate quantification because the buffer we utilize results in greater allele-specific differences in threshold cycles (see page 499, par. 1)" and "It was necessary to use HEPES buffer, pH 6.95, instead of the standard Tris-HCl, pH 8.3, for mismatch discrimination at the level shown in Figure 2". (see page 502, par. 3).

Conclusion

All claims under consideration are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suchira Pande whose telephone number is 571-272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PATENT EXAMINER
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